REMARKS

Please note that an Information Disclosure Statement and accompanying Form PTO-1449 are being filed herewith. It is respectfully requested that the cited references be considered and that an initialed copy of the PTO-1449 be returned to the undersigned attorney.

The Final Office Action mailed on April 24, 2001, has been received and reviewed. Claims 1, 2, 8, and 12-31 are currently pending in the application. Claims 1, 2, 8, and 12-31 stand rejected. Reconsideration of the referenced application is respectfully requested.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1, 2, 8, and 12-31 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, it was asserted that the specification does not provide "literal support" for the recitation of "said porous capillary column comprising a matrix including the same material as said nonporous substrate."

It is respectfully submitted that the specification does, in fact, provide support for the recitation of a matrix including the same material as a nonporous substrate. For example, page 8, line 20, of the specification states, "[w]hen a silicon substrate is employed, various techniques which are known in the art may be employed to define a porous silicon capillary column therein." The silicon of the substrate and the capillary column are the same material. As another example, page 7, lines 11-13, of the specification provides that the capillary column may comprise "porous *silicon* or hemispherical grain *silicon*", both of which are silicon, and that the capillary column "is formed on a *silicon* substrate" (emphasis supplied), again providing basis for the recitation that the matrix of the porous capillary column may be formed from the same material as a nonporous substrate.

For these reasons, it is respectfully submitted that each of claims 1, 2, 8, and 12-31 is in condition for allowance. Accordingly, withdrawal of the 35 U.S.C. § 112, first paragraph, rejections of claims 1, 2, 8, and 12-31 is respectfully requested.

Rejections Under 35 U.S.C. § 102(b)

Isaka

Claims 1, 2, 8, 14-16, 18-20, 22, 23, and 26-28 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent 5,482,598 to Isaka et al. (hereinafter "Isaka").

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Brothers v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Independent claim 1 recites a method of substantially isolating a constituent from a sample. The method of claim 1 includes, among other things, "applying the sample to a first end of a porous capillary column formed in a nonporous substrate, said porous capillary column comprising a matrix including the same material as said nonporous substrate and at least one capture substrate disposed on said matrix . . ."

While Isaka discloses a method of isolating a constituent of a sample by applying the sample to a porous capillary channel and, at col. 3, lines 6-11, that an enzyme may be immobilized at some point along the length of the porous capillary channel "to carry out various reactions", Isaka does not disclose that a sample may be applied to a porous capillary channel that includes "at least one capture substrate" disposed on a matrix thereof. Rather than act as "capture substrates" to immobilize an analyte in the sample, the enzymes disclosed in Isaka react with a substrate molecule (which is not to be confused with either a "capture substrate" or the substrate in which the porous capillary column is formed) to form a reaction product. This is true of the only two enzymes that are disclosed in Isaka: invertase (col. 3, line 8) and uricase (col. 3, line 10). Invertase hydrolyzes saccharose (col. 3, lines 8-9), while uricase reacts with uric acid (col. 3, lines 10-11). As is well known, neither invertase nor uricase "captures" the substrate molecule that is chemically altered thereby. Rather, both of the enzymes disclosed in Isaka only momentarily interact with their respective substrate molecules to produce a reaction product,

which is then released by the enzyme and is free to continue moving along the porous capillary channel.

Accordingly, it is respectfully submitted that Isaka does not disclose each and every element with the same detail provided by independent claim 1. Therefore, it is respectfully submitted that independent claim 1 is allowable under 35 U.S.C. § 102(b).

Each of claims 2, 8, and 14-16 is allowable, among other reasons, as depending either directly or indirectly from claim 1, which is allowable.

Independent claim 18 recites a method of identifying the presence of a constituent in a sample. The method of independent claim 18 includes, among other things, "applying the sample to a first end of a capillary column formed in a nonporous substrate . . .", "drawing the sample across a flowfront through said capillary column and in contact with a stationary phase disposed at a selected location along said capillary column . . .", and "detecting binding of the constituent with said stationary phase *at said selected location*." (Emphasis supplied).

Again, Isaka lacks disclosure of a stationary phase at a selected location along the porous capillary channel. For the same reasons provided above with respect to the "capture substrate" recited in independent claim 1, it is respectfully submitted that the neither of the two enzymes disclosed in Isaka could be considered a "stationary phase" that binds a constituent or that permits such binding of the constituent to be detected at the particular location of the porous capillary channel to which the enzyme is immobilized. Rather, following a reaction with appropriate substrate molecules, both of the enzymes disclosed in Isaka release a reaction product, which is then free to continue moving along the length of the porous capillary channel.

To restate, Isaka lacks disclosure of each of the following elements: applying a sample to a capillary column that includes a stationary phase disposed at a selected location thereof; binding of the constituent by the stationary phase; and detecting binding of the constituent with the stationary phase at the location of the stationary phase along the capillary column.

As Isaka fails to disclose each and every element of independent claim 18, it is respectfully submitted that independent claim 18 is allowable under 35 U.S.C. § 102(b).

Each of claims 19, 20, 22, 23, and 26-28 is allowable, among other reasons, as depending either directly or indirectly from claim 18, which should be allowed.

Claim 19 is further allowable because Isaka does not disclose a method that includes applying a sample to a capillary column with a stationary phase at a selected location therealong and "applying a detection reagent to at least said selected location and analyzing said detection reagent." The position of the Office, as stated previously, is that the *immobilized* enzyme disclosed in Isaka is the stationary phase. Thus, the *immobilized* enzyme could not also be "appl[ied] . . . to at least said selected location . . ." As Isaka does not include any further disclosure of "applying a detection reagent to at least said selected location . . .", it is respectfully submitted that Isaka does not disclose each and every element of claim 19.

Claim 20, which depends from claim 19, is further allowable since Isaka does not disclose "quantifying a change in [a] detection reagent . . ." Rather, the disclosure of Isaka is limited to quantifying the product of a reaction between an immobilized enzyme and a corresponding substrate molecule present in a sample. Accordingly, it is respectfully submitted that Isaka does not disclose each and every element of claim 20.

Claim 22 is additionally allowable since Isaka does not disclose "applying [a] stationary phase to [a] matrix" of the porous capillary channel disclosed therein. Rather, Isaka merely discloses that an enzyme such as invertase or uricase may be immobilized to the porous capillary channel. As discussed previously herein, neither of the enzymes disclosed in Isaka could be considered a stationary phase. Therefore, it is respectfully submitted that Isaka does not disclose each and every element of claim 22.

In view of the foregoing, it is respectfully requested that the Office withdraw the rejections of claims 1, 2, 8, 14-16, 18-20, 22, 23, and 26-28 under 35 U.S.C. § 102(b).

Rejections Under 35 U.S.C. § 103(a)

M.P.E.P. 706.02(j) sets forth the standard for a Section 103(a) rejection:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). (Emphasis added).

Isaka in View of Sunzeri and Swedberg

Claims 12, 13, 21, 24, 25, 30, and 31 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Isaka in view of U.S. Patent 5,536,382 to Sunzeri (hereinafter "Sunzeri") and U.S. Patent 5,571,410 to Swedberg et al. (hereinafter "Swedberg").

The nonobviousness of independent claims 1 and 18 precludes the rejections of claims 12, 13, and 30, which depend from claim 1, and of claims 21, 24, 25, and 31, which depend from claim 18, because a dependent claim is obvious only if the independent claim from which it depends is obvious. *See In re Fine,* 5 U.S.P.Q.2d 1596, 1600 (Fed. Cir. 1988); *see also* M.P.E.P. § 2143.03.

Further, it is respectfully submitted that the Office has not met its burden of setting forth a *prima facie* case as to the obviousness of any of claims 12, 13, 21, 24, 25, 30, or 31.

The teachings of Isaka are discussed previously herein.

Sunzeri teaches a method for analyzing the constituents of human biological fluids. A labeled specific binding pair member is added to a human biological fluid to effect binding between an analyte in the human biological fluid and the specific binding pair member. The constituents of the human biological fluid, including complexes of the analyte and the specific binding pair member, are separated by way of known capillary electrophoresis techniques. The separation obtained by way of capillary electrophoresis is then compared to a control, which provides a standard for quantitation by indicating the position where the analyte would have been

present if it had not been bound by the labeled specific binding pair member. The specific binding pair member is not immobilized to the matrix of the capillary electrophoresis substrate, but rather is permitted to travel therethrough with the bound analyte.

Swedberg teaches a miniaturized separation apparatus including a column within which a porous quantity of biocompatible material, such as "nylon, cellulose, polymethylmethacrylate, polyacrylamide, agarose, or the like", may be disposed. Col. 27, lines 37-40. Each of these materials have long been used in separating the constituents of biological samples. Swedberg does not teach that the porous matrix is formed in the substrate. Rather, a quantity of biocompatible, porous material is placed into an open column.

One of Ordinary Skill in the Art Would Not Have Been Motivated to Make the Proposed Combination

First, it is respectfully submitted that, none of Isaka, Sunzeri, Swedberg, or the knowledge generally available to one of ordinary skill in the art provides the motivation requisite for combining the teachings of these references and establishing a *prima facie* case of obviousness.

Isaka discloses a separation method that includes chemically altering an analyte to form a reaction product that is released by the enzyme. Accordingly, it is respectfully submitted that neither the teachings nor the suggestions of Isaka would have motivated one of ordinary skill in the art to immobilize a capture substrate or stationary phase along the capillary column thereof in such a manner that an analyte would be separated from the remainder of a sample. Moreover, Isaka would not have motivated one of ordinary skill in the art to detect the binding of an analyte to a capture substrate or a stationary phase at the location of the capture substrate or stationary phase.

While Sunzeri teaches binding of an analyte to a complementary specific binding pair member, these elements are bound before being applied to a capillary column and are not detected as a result of separation that occurs as a sample that includes the analyte flows through the capillary column and is bound to a specific binding pair member immobilized thereto. Thus,

one of ordinary skill in the art would not be motivated by the teachings or suggestions of Sunzeri to immobilize a specific binding pair member, or stationary phase or capture substrate, along a capillary column or to detect binding of an analyte to the stationary phase or capture substrate at the location of the column at which the stationary phase or capture substrate is immobilized.

Although Swedberg teaches a capillary electrophoresis separation device, the capillary electrophoresis separation device of Swedberg includes an open trench formed in a substrate and filled with a different, synthetic porous material, not with the same material as that from which the substrate is formed. Swedberg also teaches that a specific binding pair member may be secured at some location along the substrate. Nonetheless, Swedberg does not include any teaching or suggestion that would have motivated one of ordinary skill in the art to apply the teachings thereof to a separation method that involves use of a device with a substrate and a porous column formed in the substrate and including a matrix formed from the same material as the substrate. Further, due to the significant differences between the synthetic material used as the column of Swedberg from the porous silicon of Isaka, it is likely that significantly different chemistries would be required to immobilize capture substrates to the each of these materials, detracting from any motivation for one of ordinary skill in the art to combine the teachings of Isaka and Swedberg in a manner that would render obvious the application of a sample to a capillary column that comprises a matrix formed from the same material as a material of a nonporous substrate in which the capillary column is formed and that includes a capture substrate or stationary phase at a selected location thereof.

For these reasons, it is respectfully submitted that one of ordinary skill in the art would not have been motivated to combine the teachings of Isaka, Sunzeri, and Swedberg in the manner that was asserted in the outstanding Office Action.

Furthermore, based on the manner in which the teachings of these references have been combined by the Office, it appears that any such motivation to make the asserted combination could only have been based on the hindsight provided by the disclosure or claims of the referenced application.

Swedberg Teaches Away from the Proposed Combination and from the Subject Matter Recited in the Claims

Second, it is respectfully submitted that Swedberg teaches away from both the proposed combination and from the subject matter recited in the pending claims of the referenced application.

In pertinent part, M.P.E.P. § 2141.02 provides:

> A prior art reference must be considered in its entirety, i.e., as a whole, *including portions that would lead away from the claimed invention. W.L. Gore & Associates, Inc., v. Garlock, Inc.,* 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied,* 469 U.S. 851 (1984). (Italicized emphasis supplied).

Swedberg provides that the particular column substrates disclosed therein were "selected to avoid the inherent chemical activity and pH instability encountered with silicon and prior silicon dioxide-based device substrates", such as the porous silicon substrate taught by Isaka. Thus, when read by one of ordinary skill in the art, Swedberg would actually teach away from the attempted combination thereof with Isaka. Isaka and Sunzeri are both devoid of any teaching that would remedy this teaching away by Swedberg.

Further, the teaching of different column and substrate materials in Swedberg teaches away from the subject matter of the pending claims. Specifically, both independent claim 1 and independent claim 18 recite that a sample is applied to a first end of a capillary column that comprises a matrix including the same material as a nonporous substrate in which the capillary column is formed.

Therefore, it is respectfully submitted that one of ordinary skill in the art would not be motivated to combine the teachings of Swedberg with those of Isaka or with the teachings of any other reference in a manner that would render obvious the subject matter recited in the pending claims.

There Is No Reasonable Expectation that the Proposed Combination Would Be Successful

Third, it is respectfully submitted that there is no reasonable expectation that the proposed combination of Isaka, Sunzeri, and Swedberg would be successful.

In particular, it has been asserted that one of ordinary skill in the art would have been motivated to combine the teachings of these references to render obvious the application of a sample to a capillary column that comprises a matrix including the same material as a nonporous substrate in which the capillary column is formed and that includes a capture substrate or stationary phase at a selected location thereof.

When the teachings of Isaka, Sunzeri, and Swedberg are considered in their entireties, as required by M.P.E.P. § 2141.02, it is clear that the porous silicon capillary channels of Isaka could not be replaced with the porous synthetic columns of Swedberg. Independent claims 1 and 18 both require that the matrix of the capillary columns include the same material as the nonporous substrate in which the capillary columns are formed. Nonetheless, since the teachings of Swedberg are limited to the immobilization of a capture substrate to a sythetic material, in order for the proposed combination of Isaka and Swedberg to work, the porous silicon capillary channels of Isaka would have to be replaced with the synthetic material of Swedberg. Thus, the resulting structure could not include a capillary column that comprises a matrix that includes the same material as a material of the nonporous substrate in which the capillary column is formed.

For these reasons, withdrawal of the 35 U.S.C. § 103(a) rejections of claims 12, 13, 21, 24, 25, 30, and 31 as being rendered unpatentable over the combination of Isaka, Sunzeri, and Swedberg, is respectfully requested.

Isaka in View of Northrup

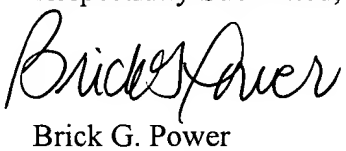
Claims 17 and 29 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Isaka in view of U.S. Patent 5,882,496 to Northrup et al. (hereinafter "Northrop").

It is respectfully submitted that claims 17 and 29 are allowable, among other reasons, as respectively depending from claims 1 and 18, which are allowable.

CONCLUSION

It is respectfully submitted that each of claims 1, 2, 8, and 12-31 is allowable. An early indication of the allowability of each of these claims is respectfully solicited, as is a notice that the case has been passed for issuance. If any issues preventing the allowance of any of claims 1, 2, 8, or 12-31 remain which might be resolved by way of a telephone conference, the Office is kindly invited to contact the undersigned.

Respectfully Submitted,



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